NATIONAL INSTITUTES OF HEALTH

FISCAL YEAR 2004

PLAN FOR HIV-RELATED RESEARCH

XI: INTERNATIONAL RESEARCH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

OFFICE OF AIDS RESEARCH

AREA OF EMPHASIS:

International Research

SCIENTIFIC ISSUES

Twenty years into the pandemic, AIDS continues to threaten virtually every part of the world. The Joint United Nations Programme on HIV/AIDS (UNAIDS) notes in its report, *AIDS Epidemic Update: December 2001*, that "AIDS has become the most devastating disease humankind has ever faced." HIV/AIDS is the fourth largest killer worldwide; in sub-Saharan Africa, it is the leading cause of death. The impact of AIDS on the developing nations of Africa, Asia, Europe, and Latin America is staggering, with even greater potential disaster to come. The cost in lost productivity and profitability, sickness and death, and a significant reduction in the skilled workforce in developing countries will have major economic impact. In South Africa, for example, the epidemic is projected to reduce the economic growth rate by 0.3–0.4 percent annually, resulting in a gross domestic product 17 percent lower than it would have been without the influence of the AIDS epidemic.

According to UNAIDS estimates:

- 40 million adults are living with HIV/AIDS; 47 percent of these are women; 2.7 million are children under the age of 15 years;
- About one-third of those currently living with HIV/AIDS are aged 15-24 and most of them do not know they are infected;
- An estimated five million new HIV infections occurred during 2001; and

- In 2001 alone, HIV/AIDS killed three million people.

As home to over 70 percent of adults and children in the world living with HIV, Africa is the region most severely affected. While encouraging signs suggest that the epidemics in sub-Saharan Africa may be stabilizing, the explosion of new infections in countries that have had low rates could reverse this trend. Epidemics are rapidly escalating in other areas of the world as well. The fastest growing epidemic is to be found in Eastern Europe, especially the Russian Federation. In this region, there were an estimated 250,000 new infections in 2001, bringing the number of people living with HIV to over one million. In Asia and the Pacific, 7.1 million people are estimated to be living with HIV/AIDS. In China alone, reported HIV infections increased by 67.4 percent in the first 6 months of 2001. Given these figures, the total number of people living with HIV/AIDS in China could be over one million. Indonesia, which for many years has not seen an escalation of new infections, has reported an increase in prevalence of HIV (from 6 to 26 percent) among sex workers. HIV rates are higher in the Caribbean and Central America than in other areas of Latin America, although Brazil and Guyana are experiencing significant epidemics. Haiti remains the most affected nation in the Caribbean, with 13 percent of pregnant women found to be HIV positive. Other countries in the region with high rates include Belize, Guatemala, and Honduras in Central America, and the Bahamas, Dominican Republic, and Trinidad/Tobago in the Caribbean.

Research to address the global pandemic is essential. Since the early days of the epidemic, NIH has supported research efforts in countries impacted by HIV and AIDS. Beginning in 1984 with a research project in Haiti and the establishment of Projet SIDA in 1985 in what was then Zaire, NIH has maintained a strong international research portfolio. Development of a research infrastructure, including training of scientists and health care providers, is an essential adjunct to these research programs. NIH has expanded its research effort to encompass more than 50 countries around the world, and collaborations between scientists in the United States and in developing countries have provided much valuable information. Results of this research benefit not only the people in countries where the research is conducted, but people affected by HIV/AIDS worldwide.

This research portfolio continues to grow and evolve in response to the continuing pandemic. In 2000, the Office of AIDS Research established a new initiative and plan for global research on HIV/AIDS. The plan was included as part of the *FY 2002 NIH Plan for HIV-Related Research* and has now become part of the annual AIDS planning process. To meet the

goals of this initiative, OAR established the NIH Global AIDS Research Strategy Group, a high-level working group comprising top officials of NIH and representatives from other governmental agencies. In addition, NIH collaborates with UNAIDS, the World Health Organization, host country governments, foundations, and nongovernmental organizations, as well as in-country scientists in the planning and implementation of the international AIDS research portfolio.

There is a pressing need in resource-poor countries for culturally appropriate and effective interventions to prevent transmission of HIV and to treat HIV and associated complications in both adults and children. Therapeutic strategies are needed for treatment of HIV with antiretroviral therapy (ART), prophylaxis, and treatment of endemic co-infections, other sexually transmitted diseases (STDs), malignancies, and neurological conditions.

An effective vaccine remains the ultimate goal to stem the pandemic, but until a vaccine is developed, other prevention interventions must be developed and implemented. Thus, NIH is pursuing international research in all these areas simultaneously. From a global perspective, the major modes of acquiring HIV infection are unprotected heterosexual intercourse and injecting drug use, with the vast majority of infections occurring through sexual transmission. Biomedical and behavioral interventions to curb this transmission in very diverse settings are urgently needed, interventions that must address specific populations at risk, such as women and adolescents. Women are particularly vulnerable and currently comprise 47 percent of adults infected with HIV worldwide. Development of prevention methods that can be controlled by women is critical. Although industrialized nations have experienced a dramatic decrease in transmission of HIV from infected mother to her child, preventing this transmission is a significant challenge in resource-poor settings of the world; strategies that can effectively be used in such settings continue to be pursued. Research also is needed to devise strategies to decrease transmission in medical settings.

INFRASTRUCTURE FOR RESEARCH ON NEW INTERVENTIONS

PRIORITY FOR FUTURE RESEARCH:

- **Develop in-country research and training infrastructure for the conduct of effective prevention and treatment interventions research, integrating new activities into existing health care and prevention services where possible.**

Various sections of the Plan describe NIH research efforts to develop vaccines for HIV; chemical and physical barrier methods, such as

microbicides, to prevent sexual transmission; behavioral strategies targeted to the individual, family, and community to alter risk behaviors associated with sexual activity and drug and alcohol use; drug and nondrug strategies to prevent mother-to-child transmission (MTCT); therapeutics for HIV-related co-infections and other conditions; and approaches to using ART in resource-poor settings. But before prevention and treatment interventions can be implemented in different geographic settings, their safety and efficacy must be demonstrated in such settings through clinical trials and other intervention research. In resource-poor countries, adequate infrastructure may not exist to conduct such trials, and it must be developed. Specific infrastructure needs include (1) developing research sites through establishment of stable, targeted cohorts, development of recruitment strategies, and enhancement of laboratory, clinical, and data management capabilities; (2) increasing the number of scientists, clinicians, and health care workers trained in basic, clinical, and behavioral research, data management, and ethical considerations; (3) developing research collaborations; and (4) transferring appropriate clinical and laboratory technologies. Critical to this effort is the need to devise innovative funding mechanisms and approaches, such as the evolving policy on provision of indirect costs to foreign institutions.

Several principles guide the development of infrastructure. Of significant importance is that many of the infrastructure needs for clinical trials are developed *through* the conduct of research in these settings, reinforcing the need to support ongoing clinical and population-based research as preparation for eventual clinical trials. In addition, infrastructure development is enhanced when the research effort is integrated with ongoing health care and prevention services and when prevention and care services themselves are integrated, enabling prevention messages to be delivered in the care setting. Other principles include involving the local community throughout the development of the research effort and ensuring a leadership role for in-country scientists.

USE OF ANTIRETROVIRAL THERAPY

PRIORITY FOR FUTURE RESEARCH:

- **Facilitate the rapid initiation of studies of the rational use and feasibility of ART in resource-diverse settings.**

The use of regimens of ART has extended the length and improved the quality of life for many HIV-infected people in industrialized countries. Unfortunately, these therapies have not been widely utilized in resource-poor nations due to factors of cost and the need for an adequate health care infrastructure to administer and monitor complex therapeutic

regimens of toxic agents. However, momentum has grown to provide options for the use of ART in these regions. It is therefore critical to move rapidly to investigate the safety and efficacy for both adults and children of various ART regimens in diverse resource-poor settings. For example, differences in diet or the use of medications for endemic diseases may alter the toxicity or the efficacy of antiretroviral drugs, as compared with industrialized areas. As the world progresses to more widely implement ART, more information is urgently needed in order to assure optimal treatment approaches. Alongside research on implementation of ART, it will be critical to conduct research related to the development of drug resistance.

In order to move rapidly in this field, the laboratory and human resource infrastructure already established in the developing world needs to be further developed specifically for treatment research, including the training of in-country scientists, clinicians, and other health care workers. In addition, low-cost approaches that can be used effectively in these settings to monitor patients for treatment efficacy and toxicity will need to be developed, including alternatives for using viral load and CD4+ cell counts, as well as lower-cost methods for these tests. The need to move rapidly will require the use of creative and flexible funding mechanisms. Finally, it is critical that dialogue is initiated early with the pharmaceutical industry concerning the provision of drugs for the research effort and for treatment regimens once they have been demonstrated safe and efficacious.

HIV-RELATED ILLNESS IN DIVERSE GEOGRAPHIC SETTINGS

PRIORITY FOR FUTURE RESEARCH:

- **Define the spectrum of HIV-related illness in diverse geographic settings and develop effective prevention and treatment interventions to limit its impact.**

Since the beginning of the epidemic in the United States, research has been conducted to characterize a variety of endemic co-infections, cancers, neurologic manifestations, and other conditions associated with HIV infection. Methods for diagnosis, prevention, and treatment of these conditions have been developed. Recently, the extensive use of effective ART has resulted in a dramatic decrease in many of these conditions. In the developing world, such conditions remain the cause of morbidity and mortality associated with HIV infection. It is necessary to develop and assess vaccines and drugs to prevent and treat them, particularly since antiretroviral drugs are only beginning to be used in these settings and may not be widely used for some time.

As a foundation for the development of such interventions, it is essential to characterize the nature, prevalence, risk factors, and course of disease for endemic co-infections, as well as other HIV-related conditions found in diverse geographic settings. An integral component is the development of diagnostic methods to detect these illnesses. The HIV-related global epidemic of tuberculosis (TB) is well documented, and the relationship with other STDs has long been understood. Considerable information about the global extent and nature of concomitant hepatitis C infection is beginning to emerge. However, little is known about other infections and conditions. It might be expected that the occurrence of conditions varies greatly depending on geography as, for example, fungal infections might prevail in one setting and bacterial infections in another. The background presence of specific cancers might affect the pattern of HIV-related cancers. Diseases not found in industrialized nations may be important in more resource-diverse regions. For example, it has been demonstrated that a fungal infection due to *P. marnefii* is a significant co-infection in Thailand, where scientists have developed an effective treatment for it. In addition, as therapies and prophylaxis strategies are developed for co-infections, it will be critical to examine the impact of new interventions on diseases not previously thought to be related to HIV but that are endemic to the region, such as malaria.

At the same time, in the United States, extended survival has been associated with the development of new conditions, some of which result from the treatment itself (e.g., metabolic disorders). As the use of ART increases in the developing world, it will be necessary to characterize conditions that emerge in these settings, since factors such as diet, the presence of endemic diseases, and the use of drugs to treat them may affect the nature and occurrence of such conditions.

DRUG AND ALCOHOL USE

PRIORITY FOR FUTURE RESEARCH:

- **Support studies to develop prevention interventions, addressing drug and alcohol use and their associated risks in transmitting and acquiring HIV infection.**

UNAIDS reports that injecting drug use is a growing factor in the AIDS epidemic, estimating that about 10 percent of HIV infections globally result from this practice. Injecting drug use is fueling epidemics in Central and Eastern Europe and countries of South and Southeast Asia, where in some countries, more than half of HIV infections are attributed to injecting drug use. As a social phenomenon, injecting drug use itself is reported to be growing in all regions of the world, including Africa. Thus the potential exists for drug-related epidemics to arise in new places and for escalation within established epidemics.

Injecting drug users who share needles and other contaminated equipment are at high risk of acquiring or transmitting HIV as well as other blood-borne infections, such as hepatitis C. However, the use of noninjecting drugs, including alcohol, also is associated with increased risk, particularly through associated sexual behavior. Of great concern is the use of alcohol and other drugs among young people. Alcohol is related to dis-inhibition, and as the most widely used drug in the world, may be associated with the spread of HIV in a variety of social contexts. For example, alcohol can be responsible for an increase in risky sexual behaviors and with the loss of inhibitions that normally guard against the use of injecting drugs. In many parts of the world, drug use and sexual transmission are inextricably linked, and drug users are more likely to be involved in the sex industry, greatly enhancing their risk of infection and the chances of HIV spreading even wider in the community. Injecting drug users are particularly vulnerable to HIV and AIDS because they are often poor and marginalized. To prevent this mode of transmission, culturally relevant interventions are needed at all levels: individual, social network, community, and society. Interventions are needed to (1) prevent the initiation of drug use; (2) prevent the transition from noninjecting to injecting drug use; (3) treat drug addiction; and (4) address the transmission of other infections through the same routes, such as hepatitis C. To ensure that newly developed interventions are culturally appropriate, it is critical to conduct research to better understand the social context of drug and alcohol use and to involve the community at all levels of the research.

STIGMA AND HEALTH BEHAVIORS

PRIORITY FOR FUTURE RESEARCH:

- **Study the interrelationships between stigma and health behaviors such as seeking and/or utilizing prevention and treatment interventions and devise strategies to improve access to and uptake of interventions.**

Since the earliest days of the epidemic, stigma has been associated with AIDS in virtually every setting. Much of this stigma is related to the modes of transmission, and its impact is evident at government, societal, family, and individual levels. Government leaders have been reluctant to acknowledge the presence of an AIDS epidemic; communities have shunned entire social groupings because of association with AIDS; families have rejected HIV-infected family members or hidden their illness; and individuals have been reluctant to disclose their status for fear of discrimination in all aspects of their lives. Stigma prevents infected individuals from seeking or utilizing prevention and care services even where they are available, which impacts negatively on their own health

and the health of their sexual partners and family members. Stigma also prevents individuals from using prevention strategies even when they are simple, affordable, and practical. Thus stigma fuels the epidemic by inviting the further spread of HIV infection. In many resource-poor areas of the world, stigma extends into the next generation and makes more difficult the lives of those already struggling under overwhelming odds—AIDS orphans.

Research is needed to better understand how to combat stigma at all levels. Within this broad context, a focus for NIH is identifying factors that act as barriers to or facilitators for seeking prevention and care services, as well as utilizing known prevention strategies. Because the cultural context of stigma varies widely throughout the world, research must seek to define the relevant context for any given geographical area in identifying barriers and designing strategies to address them. Questions include the role of stigma in whether infected individuals seek treatment and care, and, with the advent of more treatment options in resource-poor settings, the reverse question of whether expanded care will lead to a decrease in stigma. Research also is needed to identify models to encourage people to access voluntary counseling and testing. Other research questions related to individual behaviors that can directly impact on the risk of HIV transmission are using condoms or microbicides; seeking treatment for other STDs; and using alternatives to standard breast-feeding practices.

OPERATIONAL RESEARCH

PRIORITY FOR FUTURE RESEARCH:

- **Develop capacity and support for operational and health services research to facilitate the translation of research findings to clinical practice and public health programs in resource-diverse settings.**

To combat the pandemic, it is essential to implement the results of research that have an impact on affected populations. Information gained through research must be translated into activities that will enhance patient management, improve prevention programs, and inform policy decisions in resource-poor settings around the world. Further, ethical issues must be considered in planning for implementation of research results. Accomplishing these goals requires that research results be made available to policymakers in foreign governments, as well as to nongovernmental organizations and international organizations that develop programs to deliver health care, prevention, and other services. In addition, research results must be interpreted in the context of the host country's social, cultural, economic, and political situation. Finally, many decisions must be made about establishing new or modifying existing treatment and prevention programs. To facilitate this process, the conduct of operational

research is of critical importance, to better understand how to develop and implement programs in the relevant country context.

Issues that need to be addressed include local logistical problems; social and behavioral risks for transmission specific to each regional population; regional economic and political realities; long-term sustainability of treatment and care infrastructure, prevention programs, and study cohorts; and ethical issues within cultural realities. Of specific concern is the need to ensure maintenance of prevention efforts while implementing ART in these settings. Examples of specific topics for study include how best to provide prevention services in the care setting; the cost-effectiveness of voluntary counseling and testing to enhance access to care and prevention services; and the economic impact of ART on individuals, families, and communities.

Central to this effort is the conduct of operational research on how to scale up interventions from cohorts in trials to provide widespread delivery of interventions through community-wide or country-wide programs, as well as how to scale up from early studies to large-scale trials. In some cases, it may be desirable to address the needs of a geographic region as a whole. This research must be interdisciplinary, encompassing clinical, behavioral, and health services research, including an emphasis on cost-effectiveness of various approaches to scaling up.

In order to conduct operational research, it is necessary to build capacity for the integration of clinical, operational, and health services research, including training of foreign investigators in translational and operational research, with a focus on implementation and evaluation of prevention intervention strategies and treatment approaches, as well as feasible, cost-effective surveillance systems.

ETHICAL CHALLENGES

PRIORITY FOR FUTURE RESEARCH:

- **Address ethical, legal, and human rights challenges in research and implementation of research findings in resource-diverse settings.**

Ethical considerations must be paramount in the development of international collaborations and NIH support of research activities in other countries. Central to this concept is the requirement that research must be relevant to the country where the research is conducted and that the results of research must be translated into relevant programs. Partnerships among scientists, between governments, and with nongovernmental and international organizations are key. Involvement of in-country policymakers and community representatives, as well as

scientists and service providers, is essential to ensuring that research is appropriate to the setting. Research relevant to war-torn areas presents a particular challenge.

It is universally accepted that researchers should adhere to and address standard ethical principles in the design and conduct of research. Essential to the protection of human subjects participating in research, these principles are outlined in several documents and include respect for persons, beneficence, and justice. However, the vastly different economic and cultural contexts in which research is conducted in international settings create many challenges for researchers and funding agencies in the application of these principles. For example, obtaining voluntary informed consent from each study participant may be complicated in some settings by social customs requiring the involvement of others in the community in this process, such as family members or community leaders. Differences in law, regulation, and public policy, as well as organizational structures, mean that careful consideration must be given to how ethical standards of both the United States and the country where research is conducted can be met. To ensure that research is appropriate to the setting, relevant to the prevailing standard of care, and responsive to cultural issues, it is essential that proposed studies receive full ethical review and approval in the country where the research will be conducted, as well as in the United States. Unfortunately, many resource-poor nations do not have mechanisms in place to conduct ethical review. Thus, a critical component of research infrastructure is strengthening the capability of countries to conduct their own independent ethical review of research.

Integral to addressing ethical considerations is ensuring a leadership role for foreign scientists in the countries where studies are conducted. In development of collaborations, they must be full and equal partners in the design and conduct of studies and have full responsibility for the conduct of studies in-country. This responsibility should include full participation in the conceptualization of the research; development of protocols; study implementation and collection of data; data processing and analysis; and dissemination of information about the research and its results, through the press, professional meetings, and publications in scientific journals.

SCIENTIFIC OBJECTIVES AND STRATEGIES

OBJECTIVE - A:

Build research capacity in international settings that will: (1) provide an environment that promotes the development of equal partnerships between U.S. and foreign investigators; (2) facilitate the conduct of basic biomedical and behavioral research and long-term cohort studies; (3) serve as loci for studies of prevention interventions (biomedical and behavioral) and the safety and efficacy of therapeutic biomedical and behavioral prevention interventions (including Phase I, II, III, and IV trials of vaccines, microbicides, and therapies); (4) train investigators from throughout the region; and (5) provide linkage with programs that provide services.

STRATEGIES:

Site Development

- Develop new and improve existing international research sites as rapidly as possible, addressing geographic regions and specific populations where HIV is and/or will be a major cause of morbidity and mortality.
- Enhance capacity for the conduct of basic and applied research, clinical trials, and studies of clinical aspects of HIV and related conditions, with emphasis on good clinical practices of the intensity and rigor needed for large-scale trials through:
  - conducting ongoing incidence assessments in a variety of risk segments of the population;
  - enhancing laboratory capacity with appropriate quality control;
  - developing affordable alternatives to viral load and CD4+ cell counts for monitoring treatment efficacy and toxicity;
  - developing clinical capabilities;
  - improving capacity for voluntary counseling and testing;
  - funding the use of existing databases to study the natural history of HIV disease;
  - enhancing data collection and analysis capabilities;
  - funding the analysis of existing international databases and developing common data elements for new databases;

  - addressing problems in maintaining repositories of biological samples in developing countries, such as loss of electrical power to keep samples frozen;
  - developing strategies for recruitment and retention of participants into treatment and prevention studies;
  - developing strategies for maintaining adherence and followup studies of participants; and
  - enhancing the ability to assure protection for human subjects involved in research and the ethical conduct of research.
- Build global capacity to support the integration of clinical, operational, and health services research.
- Conduct studies of incidence and feasibility in order to identify at least 60 sites suitable for the conduct of efficacy trials of HIV prevention interventions.

Training

- Continue to support training of clinicians, public health professionals, and scientists from developing nations to enhance the conduct of research on HIV, AIDS, STDs, and other HIV-related co-infections and malignancies, including training in (1) clinical aspects, (2) treatment and care (e.g., clinical trials of therapeutic strategies for HIV and endemic co-infections), (3) development and testing of vaccine candidates, (4) impact of alcohol and other substance abuse/dependence on HIV transmission, (5) disease progression, and (6) other biomedical and behavioral prevention research.
- Enhance training in translational and operational research, including implementation and evaluation of prevention intervention strategies, treatment approaches, and feasible, cost-effective surveillance systems.
- Provide training in data management and analysis for in-country research personnel.
- Develop in-country training partnerships and support "south-to-south" training to (1) enable investigators to obtain training appropriate for the areas in which they will work, and (2) enable trained investigators returning to their home countries to serve as training resources for other scientists in their own countries and geographic regions.

- Enhance training to develop clinical capability and to facilitate technology transfer, including the delivery of ART.
- Provide training to ensure that clinicians and other health care workers understand infection control principles and can implement proper procedures in resource-poor settings.
- Ensure training that specifically includes the requirements of "good clinical practices."
- Provide training and technical assistance in the preparation and successful application of grant proposals.
- Provide training in manuscript writing.
- Implement mechanisms to overcome language barriers so that investigators in non-English-speaking countries could have more open access to NIH grants.
- Expand training to address research administration, fiscal accountability, research support services, and grants management.

Collaboration and Coordination

- Enhance coordination of NIH international research efforts.
- Coordinate NIH AIDS and non-AIDS research efforts, particularly where projects are active in the same country and/or region.
- Encourage the continued development of collaborations between international and U.S. investigators, ensuring that research projects are relevant to strategic planning at the local level, to maximize the research effort in resource-limited settings.
- Support mechanisms, such as "re-entry grants," to fund research activities of trained foreign investigators returning to their countries.
- Ensure the leadership role of in-country investigators and policy-level individuals in countries where studies take place by involving them in all stages of the research, including conceptualization of the research question, study design, development of protocols, study implementation and collection of data, data analysis, publication and presentation of research results, and interaction with the media.
- Provide assistance to foreign collaborators in addressing regulatory issues and special oversight mechanisms.

- Work with other U.S. governmental agencies, foreign governments, international organizations, nongovernmental organizations (NGOs), Global Fund for AIDS, TB, and Malaria (GFATM) recipients, and industry to facilitate development and testing of vaccines, microbicides, drugs, and other prevention strategies, including behavioral interventions.

- Work with other U.S. governmental agencies, foreign governments, international organizations, NGOs, and industry to make available to study participants and host-country populations effective interventions that result from research.

- Explore collaboration with indigenous health providers to facilitate accomplishment of research objectives, including enhancing the participation of indigenous populations in research and improving understanding of the complexities of addressing diseases in diverse geographical settings.

- Develop programs to foster understanding of science, the role of research and attendant ethical issues and thereby enhance reporting of AIDS issues relative to geographical areas heavily impacted by the pandemic by (1) strengthening the skills of in-country and U.S. scientists in communicating effectively to the media and (2) educating the media to report on health research issues.

- Train policymakers in using research to affect policy.

Ethical Issues

- Ensure that research projects are designed to benefit the countries in which the research is being conducted.

- Enhance the capability of foreign institutions to conduct independent scientific and ethical reviews.

- Ensure education/cross-fertilization between developing country ethical review committees and U.S. institutional review boards (IRBs), and educate IRBs about cultural issues in developing countries.

- Ensure the participation of local communities, NGOs, and governments in the development of research protocols.

- Ensure that ethical challenges in both research and the implementation of research results in resource-limited settings are clearly described and addressed in grant proposals.

- Consider the need for study participants and their communities in host countries to have maximum possible access to any preventive or therapeutic products developed during the research, and initiate dialogue with pharmaceutical companies early in the clinical trials planning process in resource-limited settings.
- Ensure confidentiality of information about HIV-infected substance abusers, including information on individuals in treatment for substance abuse.
- Conduct research designed to identify ways to improve the application of ethical principles in the conduct of research.
- Include a certain percentage of individuals as members of AIDS study sections who know the importance of cultural factors and/or those who have worked in developing countries.
- Consider allowing local models of human subjects review in foreign countries to be accepted as equivalent to U.S. standards.
- Fund studies on new models for IRB review.
- Ensure that ethical review mechanisms, such as consent forms, are relevant to the country where the research is conducted and are placed in cultural context.
- Conduct workshops on ethical principles and their implementation in research, encouraging countries to develop their own set of ethical guidelines and procedures, to include the principles of respect for persons; beneficence; justice; and the application of informed consent, assessment of risks and benefits, and selection of subjects.
- Conduct training in ethical issues and how to address them in grant applications.
- Encourage in-country scientists and leaders to work closely with local journalists to foster understanding of science, the role of research, and attendant ethical issues.

Technology Transfer

- Provide improved access to information through enhanced information technology.

- Transfer clinical and laboratory technologies that may be sustained and used for implementation of prevention, symptom management, and patient care programs once research studies are completed.

Funding Mechanisms

- Develop creative and innovative approaches and mechanisms to provide funding for infrastructure development and for rapidly launching clinical trials, including improvement of space for confidential counseling, clinical care, and laboratory investigations.
- Design flexible and rapid mechanisms to permit conduct of expanded prevention clinical trials when preliminary studies indicate that a product or approach merits full-scale evaluation.
- Continue to explore new funding approaches for international research, including direct funding of overseas investigators and provision of indirect costs to foreign institutions.
- Continue to address indirect cost issues.

OBJECTIVE - B:

Establish the most effective, affordable, and practical ways to care for HIV-infected adults, adolescents, and children in resource-limited settings, including treatment of HIV and related conditions, such as endemic co-infections, malignancies, other STDs, neurological conditions, and nutritional deficiencies.

STRATEGIES:

Treatment of HIV with Sustainable Antiretroviral Therapy

- Determine affordable, safe, and effective ART regimens, including timing of initiation and appropriate drugs, that can be used in diverse resource-poor geographic settings.
- Determine cost-effectiveness of antiretrovirals (ARVs) in developing countries.
- Determine the pharmacokinetics of ARVs in various populations, including children.
- Investigate the impact of co-infections with other endemic diseases on the use of ART.
- Study drug-drug interactions among ARVs, medications for other endemic diseases, and medications or substances used for nonmedical reasons, as well as interactions with vaccines in standard use.
- Investigate interactions between HIV therapeutics, drugs of abuse, or medications used for the treatment of substance abuse in pregnant women; evaluate the impact of such interactions on the maintenance of anti-addiction therapy and on MTCT.
- Study the impact of the use of nevirapine for preventing MTCT on response to ARVs in women who subsequently receive non-nucleoside reverse transcriptase inhibitor-containing highly active antiretroviral treatment (HAART) regimens.
- Support the long-term followup of children exposed to ART during pregnancy and/or postpartum to evaluate possible late effects of exposure.
- Study treatment efficacy, side effects, and toxicity of ARVs in pediatric populations.

- Study drug compliance in children, especially as they move into and through adolescence.
- Determine the safest and most efficient diagnostic strategies and treatment modalities for endemic co-infections (especially for those not commonly found in the United States) in the pediatric/adolescent populations.
- Assess the impact of nutritional status and nutritional interventions on patient survival and the efficacy and tolerability of ART.
- Study the impact of nutritional supplementation on the rate of immune system deterioration in HIV-infected persons in relation to ART.
- Determine the efficacy of ART regimens on various clades prevalent around the world.
- Examine the potential use of HIV vaccines in the context of suppressive ART.
- Study the impact of HIV vaccines on HIV disease progression in relation to initiation of ART.
- Develop and evaluate suitable, sustainable approaches for monitoring treatment efficacy, side effects, and toxicity, with particular emphasis on finding affordable CD4+ cell counts and HIV load methodologies and suitable alternatives.
- Determine the impact of ART on development of drug-resistant strains of HIV in diverse geographical settings.
- Assess the impact of ART on HIV transmission and prevalence in various communities.
- Determine the social, psychological, societal, and economic impact of ART on individuals (including children), families, and communities, including impact on personal risk behavior.
- Examine the effectiveness of various approaches to the administration of therapy (e.g., directly observed therapy or directly delivered therapy).
- Identify conditions that emerge as a consequence of ART and longer survival, such as malignancies, neurological and neuropsychological conditions, and metabolic and nutritional dysfunction.

- Determine whether expanded antiretroviral care and ART lead to a decrease in HIV-associated stigma.
- Develop strategies to ensure that prevention efforts in resource-limited countries are simultaneously preserved and enhanced when clinical trial, and later ART treatment, programs are established.

Sustainable Strategies for Preventing and Treating Endemic Co-infections and Other HIV-Related Conditions

- Define the spectrum, incidence, and risk factors for HIV-related illnesses (e.g., endemic co-infections, malignancies, and neurological conditions) specific to individual regions in diverse geographic settings.
- Develop simplified diagnostic tests for endemic co-infections and other conditions, such as hepatitis C virus (HCV).
- Investigate sustainable strategies for preventing, treating, and monitoring response to treatment of endemic co-infections and other HIV-related conditions.
- Assess the impact of available antibiotic treatment and prophylaxis regimens to optimize therapeutic approaches for TB and other endemic co-infections.
- Study drug-drug interactions among drugs used to prevent and treat endemic infections.
- Develop simple clinical algorithms for guiding initiation of prevention or treatment of infections.
- Identify affordable means to target high-risk patients for initiation of prophylaxis.
- Develop methods to monitor development of antimicrobial resistance by HIV-related and endemic pathogens infecting both study participants and the general population.
- Identify strategies to limit development of drug resistance.
- Develop strategies to enhance and monitor adherence to therapy/prophylaxis for endemic co-infections.
- Determine the safety and effectiveness of available immunizations in diverse HIV-infected populations.

- Assess the burden of TB and the relative importance of reactivation versus *de novo* infection in various settings.

Approaches to Care

- Determine barriers and facilitators to acceptance of HIV testing and treatment and/or prevention reocmmendations.
- Develop culturally appropriate mechanisms to identify persons for whom treatment is indicated, and to overcome factors such as stigma, which can forestall testing and limit the provision of treatment and care.
- Continue to identify better, low-cost alternatives for diagnosis of HIV.
- Develop better approaches to voluntary counseling and testing that encourage knowledge of one's status and help mitigate social harm.
- Identify clinical management approaches, including effective palliative care strategies, and overall care needs among HIV-infected persons in diverse settings.
- Develop care models and enhance interdependent care services that integrate AIDS care into existing programs, such as TB control programs, alcohol and other substance abuse/dependence treatment programs, and maternal and child health services, to avoid duplication of efforts.
- Develop TB prevention and education strategies for use with HIV-infected individuals, as well as the general population.
- Develop interventions to mitigate the negative social consequences of HIV infection, including AIDS stigma, with particular emphasis on children affected by or infected by HIV (AIDS orphans).

Crosscutting Strategies

- Continue to characterize the natural history of HIV infection in diverse geographic settings.
- Examine the role of co-infections with other endemic diseases in modulating HIV, including risk of acquiring and/or transmitting infection and disease progression.

OBJECTIVE - C:

Develop and evaluate biomedical and behavioral prevention interventions appropriate for use in diverse geographical settings.

STRATEGIES:

Blood-Borne Transmission

- Evaluate the risk of transmission of HIV and other blood-borne pathogens through contaminated blood and medical accidents.
- Develop strategies to prevent blood-borne transmission in health care settings, including recruitment and retention of appropriate blood donors, predonation counseling of all blood donors, improvement of blood screening strategies and technologies, and appropriate use of transfusion.
- Encourage research on the relationship between the use of paid and/or professional blood donors and the dynamics of the spread of HIV infection.
- Encourage research on the role of plasma and the spread of HIV infection.
- Develop strategies to improve implementation of universal precautions.
- Develop strategies to prevent blood-borne transmissions through misuse of injections in and outside the health care setting.

Sexual Transmission

- Establish the most effective and sustainable ways to change or prevent high-risk sexual behaviors, such as multiple partners, rape, trafficking of women and children into forced sex work and commercial sex work, and substance use and abuse that foster the spread of HIV and STDs in resource-limited settings.
- Develop strategies to prevent HIV transmission by high-risk sexual behaviors, including the continued development of microbicides; studies of other preventive strategies, such as barrier methods and the factors affecting their use; syndromic management of STDs; and the cost-effectiveness of such strategies.

- Investigate the effectiveness of community-based and community-level HIV prevention programs, including prevention education based on abstinence and monogamous relationships and strategies to evaluate, replicate, and extend effective behavioral interventions.
- Perform research into the culturally appropriate content, form, and format of instruments that will improve the quality of culturally appropriate self-reports of sexual risk behaviors.
- Develop biomedical and behavioral strategies to prevent high-risk sexual behavior transmission of STDs, with particular emphasis on women and adolescents.
- Improve clinical management of viral sexually transmitted infections, emphasizing co-infections with human simian virus (HSV)-2 and human papillomavirus (HPV).
- Study gender-related biological factors affecting susceptibility to infection, including the use of hormonal contraceptives and the presence of gender-specific conditions, such as HPV and cervical cancer.
- Examine the role of co-infection with other endemic diseases in modulating HIV, including risk of acquiring and/or transmitting infection and disease progression.

Substance Use

- Investigate the role of alcohol and other commonly used psychoactive substances in promoting sexual risk behaviors and as intervening factors that act as barriers to prevention, reduce the efficacy of prevention strategies, and enhance other risks for HIV, such as STDs.
- Investigate the impact of alcohol, drug abuse, and other associated co-morbid conditions on HIV disease progression, adherence to treatment regimens, and clinical outcomes.
- Devise strategies to prevent initiation of drug use, alcohol dependence, and transition to riskier drug practices, such as initiating injection.
- Conduct studies to identify sustainable interventions at the levels of the individual, social network, community, and society to prevent HIV transmission as a result of high-risk sexual activity and/or drug use practices associated with alcohol and drug use.

- Evaluate innovative, culturally relevant, contextually appropriate substance use treatment programs for their utility as HIV prevention approaches in different international settings.
- Determine the factors involved in the injecting and noninjecting drug user's social networks that influence the rate and patterns of diffusion of HIV infection, and design prevention programs based on the results.
- Conduct comparative epidemiological studies of substance use and HIV risk in settings of varying cultural conditions and HIV seroprevalence.
- Evaluate the risk of transmission through injecting drug use with respect to the availability of sterile needles and syringes.

Mother-to-Child Transmission

- Develop safe, effective, feasible, and conveniently administered strategies to interrupt MTCT, using interventions that are affordable and can be implemented in resource-poor nations, including specific strategies to prevent postnatal transmission of HIV through breast milk by providing prophylaxis to the infant, mother, or both during the lactation period.
- Develop and evaluate strategies for reducing the risk of MTCT without compromising treatment of the pregnant woman.
- Study the effect of ARV regimens used for maternal health indications on the risk of MTCT (including postnatal transmission through breast milk) and other outcomes, including pregnancy outcomes.
- Investigate the mechanisms and timing of MTCT (*in utero*, intrapartum, and postpartum via breast milk) to facilitate and develop targeted drugs/strategies to further decrease MTCT or provide alternatives to currently identified effective strategies.
- Further identify cost-effective, nondrug regimens for preventing MTCT, including research on infant feeding and treatment of reproductive tract infections.
- Conduct studies to evaluate and reduce short- and long-term toxicity of antiretroviral drugs in women during pregnancy and in their offspring who were perinatally exposed.

- Investigate the unique immune status and develop immune interventions in both pregnant women and infants to interrupt HIV transmission.

- Examine the role of maternal and infant nutrition during the peripartum and postpartum periods in reducing morbidity and mortality in HIV-infected mothers and their infants and in reducing MTCT.

- Study the impact of the health status of HIV-infected mothers on the survivability of both HIV-infected and noninfected children.

- Study the impact of breast-feeding on the health status of HIV-infected mothers.

- Devise strategies to develop or use existing infrastructures to identify women at risk of HIV infection, and to implement treatment of them.

Vaccine Development

- Continue the accelerated efforts toward development of vaccine candidates suitable for use around the world, and foster the development of vaccines to optimize characteristics appropriate for broad international use, including designs exhibiting low cost with ease of production and administration, as well as stability.

- Define immune approaches that will provide specific and sustained protection against HIV transmission; develop the products necessary to achieve these goals; and develop the capacity to evaluate their safety in human subjects.

- Provide a solid scientific knowledge base (incidence, viral subtypes, major histocompatibility [MHC] types, natural history) to justify clinical trials in international sites; and to conduct trials in these sites and communities according to the highest clinical and ethical standards.

- Identify suitable populations of adults and children in which to evaluate candidate vaccines.

- Conduct Phase I, Phase II, and Phase III trials for safety, immunogenicity, and efficacy with suitable candidate vaccines or concepts in domestic and international settings.

- Enlist participation of local representatives in the development of appropriate trials protocols as well as responsive mechanisms to inform and educate the participating individuals; establish networks within the community that will effectively, and on a continuing basis, address the social and medical concerns of the participants; establish mechanisms to provide ongoing information; and open discussions concerning the scientific rationale of the study.

- Examine relevant behavioral issues related to the conduct of vaccines research and acceptability in diverse populations.

- Conduct research on the social and economic impact of vaccines and their cost-effectiveness.

Crosscutting Strategies

- Develop sustainable behavioral, economic, and environmental interventions to address the multiple risk factors present in selected populations.

- Conduct multidisciplinary prevention research in multiple settings, including medical treatment and community support and care organizations, based on rapid assessments of at-risk groups identified in each local geographic context.

- Conduct research to integrate the multiple components of diverse issues of sexuality, alcohol and other substance use, and mental health into HIV prevention programs.

- Encourage research on the impact of integration of prevention and care services and the organization of health services at the public health level, including evaluation, dissemination, and expansion of model programs.

- Develop new approaches to voluntary counseling and testing and assess them for cost-effectiveness and impact on reducing risk from sexual behavior and drug use in settings with varying levels of seroprevalence.

- Study gender-related social and behavioral factors affecting acquisition of infection, such as economic power imbalances between the sexes.

- Evaluate strategies to reduce stigma and increase willingness of individuals (1) to enter into voluntary counseling and testing, (2) to identify, accept, and undertake alternative infant feeding practices, and (3) to enter ART.

- Develop biomarkers that can serve as surrogates for measurement of HIV risk behavior and can be used to predict and monitor rapid escalation of HIV epidemics.
- Identify biological determinants of infectiousness and susceptibility to infection, including both viral and host factors.
- Study gender-related biological factors affecting susceptibility to infection, including the use of hormonal contraceptives and the presence of gender-specific conditions such as HPV and cervical cancer.
- Utilize population-based studies to examine basic scientific questions about HIV, its transmission, and host response, including viral evolution, viral diversity, and human immunology.
- Conduct research on how best to deliver prevention education in the care setting.

OBJECTIVE - D:

Enhance the translation of research results for the improvement of patient management, development of prevention programs appropriate to the setting, and to inform policy decisions in resource-poor settings around the world by conducting translational and operational research on implementation, including: (1) local logistical problems, (2) social and behavioral risks of HIV transmission specific to each regional population, (3) regional economic and political realities, (4) long-term sustainability of research infrastructure and cohorts, (5) full community participation in research planning and implementation, and (6) ethical issues within cultural realities.

STRATEGIES:

- Conduct translational and operational research to accomplish widespread delivery of interventions to prevent transmission and acquisition of HIV infection and to provide care and treatment for those individuals and families affected by HIV (e.g., (1) ART; (2) HIV vaccines; (3) microbicides; (4) treatment and prophylaxis of endemic co-infections, including TB; (5) other products; and (6) behavioral and other interventions, such as syndromic management of STDs and breast-feeding practices, including logistical issues on how to scale up from research projects; and (7) substance abuse treatment).
- Continue to characterize behavioral, social, and structural risk factors (including cross-border issues) for transmission of HIV in specific populations and geographic areas.
- Conduct research on how to scale up from pilot projects and/or early Phase I and II trials to large research populations, including Phase III trials.
- Conduct research on how to scale up from research studies to implementation of programs.
- Develop criteria for different aspects of sustainability of potential interventions that can be used to determine priorities for research.
- Educate investigators to address sustainability of technologies in grant proposals.
- Integrate operational and health services research with clinical research to facilitate the translation of research findings into clinical practice and public health programs, addressing HIV in the context of other diseases, access to health care, and prevention programs.

- Identify models for sustainability; integrate research with sustainable treatment and care by coordinating U.S. efforts with those of other governments, the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), the U.S. Agency for International Development (USAID), NGOs, and recipients of funding from the GFATM.
- Develop models for communication among agencies.
- Ensure the integration of U.S. research programs with established country programs, including collaboration with local investigators on strategic planning.
- Involve developing country partners, including policymakers and Ministries of Health, as well as local investigators, in design of clinical trials and endpoints through continuing community advisory board development and strengthening.
- Develop meaningful community participation at the initiation of development of research.
- Develop regional approaches to research (e.g., through regional meetings) to enhance communication and to address common problems and needs among countries in the region.
- Facilitate development of HIV prevention and treatment guidelines, adding behavioral, basic, and epidemiological aspects to clinical findings.
- Provide improved access to information concerning treatment and prevention guidelines and the results of research through enhanced information technology.

APPENDIX A:

NIH Institutes and Centers

NIH INSTITUTES AND CENTERS

NCI	National Cancer Institute
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NHGRI	National Human Genome Research Institute
NIA	National Institute on Aging
NIAAA	National Institute on Alcohol Abuse and Alcoholism
NIAID	National Institute of Allergy and Infectious Diseases
NIAMS	National Institute of Arthritis and Musculoskeletal and Skin Diseases
NICHD	National Institute of Child Health and Human Development
NIDCD	National Institute on Deafness and Other Communication Disorders
NIDCR	National Institute of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NINDS	National Institute of Neurological Disorders and Stroke
NIDA	National Institute on Drug Abuse
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIMH	National Institute of Mental Health
NINR	National Institute of Nursing Research
NLM	National Library of Medicine
CC	Warren Grant Magnuson Clinical Center
CIT	Center for Information Technology
NCCAM	National Center for Complementary and Alternative Medicine
NCRR	National Center for Research Resources
FIC	Fogarty International Center
CSR	Center for Scientific Review
NCMHD	National Center on Minority Health and Health Disparities
NIBIB	National Institute of Biomedical Imaging and Bioengineering

APPENDIX B:

FY 2004 OAR Planning Group for International Research

FY 2004 INTERNATIONAL RESEARCH PLANNING GROUP

Non-NIH Participants

Laura Guay, M.D., Co-Chair
Associate Professor of Pathology/Pediatrics
Department of Pathology
Johns Hopkins University

Susan Allen, M.D., M.P.H., D.I.M. & H.
Associate Professor
University of Alabama at Birmingham

Chris Beyrer, M.D., M.P.H.
Director
Fogarty AIDS International Training and Research Program
Johns Hopkins University

Deborah L. Birx, M.D.
Director
U.S. Military HIV Research Program
Walter Reed Army Institute of Research

Carlos del Rio, M.D.
Associate Professor of Medicine
Division of Infectious Diseases
Emory University School of Medicine

David D. Celentano, Sc.D.
Professor
Johns Hopkins Bloomberg School of Public Health

Farley R. Cleghorn, M.D., M.P.H.
Assistant Professor of Medicine and Epidemiology
Institute of Human Virology
University of Maryland

Roger Detels, M.D., M.S.
Professor and Chair
Department of Epidemiology
School of Public Health
University of California, Los Angeles

Patricia Fast, M.D., Ph.D.
Director, Medical Affairs
International AIDS Vaccine Initiative

Mr. Gregg Gonsalves
Director of Treatment and Prevention
Gay Men's Health Crisis

Jonathan E. Kaplan, M.D.
Associate Director for Opportunistic Infections
Division of HIV/AIDS Prevention
Centers of Disease Control and Prevention

David Katzenstein, M.D.
Associate Professor of Medicine
Division of Infectious Diseases
Stanford University

Sanjay Mehendale, M.D., M.P.H.
Deputy Director
National AIDS Research Institute, India

Michael H. Merson, M.D.
Dean of Public Health
Department of Epidemiology and Public Health
School of Medicine
Yale University

Sophia Mukasa Monico, LL.B.
International Council of AIDS Service Organization, Canada

Luwy Musey, M.D.
Associate Director
Merck Research Laboratories

Jean William Pape, M.D.
Professor of Medicine
Director, Gheskio Center
Cornell University, Haiti

Christopher V. Plowe, M.D., M.P.H.
Associate Professor and Head
Malaria Section
Center for Vaccine Development
School of Medicine
University of Maryland

Zeda F. Rosenberg, Sc.D.
Scientific Director
HIV Prevention Trials Network
Family Health International

Jie Shen, M.Sc.
Vice President
Chinese Academy of Preventive Medicine
Director
National Center of HIV/AIDS Prevention and Control
Chinese Academy of Preventive Medicine, China

Ramon Jeremias Soto, M.D., M.H.S.
Regional Coordinator
Multicenter Study on HIV/STI
PASCA and National Autonomous
University of Honduras, Honduras

Taha E. Taha, M.D., Ph.D.
Associate Professor
School of Hygiene and Public Health
Johns Hopkins University

Catherine M. Wilfert, M.D.
Scientific Director
Elizabeth Glaser Pediatric AIDS Foundation

Zunyou Wu, M.D., Ph.D.
Research Scientist and Professor
Director
Department of Health Education and Behavioral Intervention
National Center for AIDS/STD Control and Prevention
Chinese Center for Disease Control and Prevention, China

NIH Participants

Ms. Linda Reck, Co-Chair
Senior Policy Analyst
Office of AIDS Research, NIH

Jodi Black, Ph.D.
Program Director
National Cancer Institute, NIH

Kenneth Bridbord, M.D., M.P.H.
Director
Division of International Training and Research
Fogarty International Center, NIH

Henry "Skip" Francis, M.D.
Director
Center on AIDS and Other Medical Consequences of Drug Abuse
National Institute on Drug Abuse, NIH

Christine Grady, R.N., Ph.D.
Head
Section on Human Subjects Research
Department of Clinical Bioethics
Warren G. Magnuson Clinical Center, NIH

Rodney Hoff, D.Sc., M.P.H.
Senior Epidemiologist for International Research
Division of AIDS
National Institute of Allergy and Infectious Diseases, NIH

Barbara Laughon, Ph.D.
Chief
Opportunistic Infections Research Branch
Division of AIDS
National Institute of Allergy and Infectious Diseases, NIH

Susan F. Newcomer, Ph.D.
Statistician (Demography)
Demographic and Behavioral Sciences Branch
Center for Population Research
National Institute of Child Health and Human Development, NIH

Leslie K. Serchuck, M.D.
Medical Officer
Pediatric, Adolescent and Maternal AIDS Branch
National Institute of Child Health and Human Development, NIH

Ellen Stover, Ph.D.
Director
Division of Mental Disorders, Behavioral Research and AIDS
National Institute of Mental Health, NIH

APPENDIX C:

List of Acronyms

LIST OF ACRONYMS

ART	antiretroviral therapy
ARV	antiretroviral
ACTIS	AIDS Clinical Trials Information Service
AIDS	acquired immunodeficiency syndrome
AITRP	AIDS International Training and Research Program, FIC
ATI	Analytic Treatment Interruption
ATIS	HIV/AIDS Treatment Information Service
BSL	biosafety level
B/START	Behavioral Science Track Award for Rapid Transition
CAB	community advisory board
CAPS	Center for AIDS Prevention Studies (University of California, San Francisco)
CBO	community-based organization
CDC	Centers for Disease Control and Prevention
CFAR	Center for AIDS Research
CIPRA	Comprehensive International Programs for Research on AIDS
CMS	Centers for Medicare and Medicaid Services
CMV	cytomegalovirus
CNS	central nervous system
CSF	cerebrospinal fluid
CTL	cytotoxic T lymphocyte
DC	dendritic cell
ddI	dideoxyinosine
DHHS	Department of Health and Human Services
DNA	deoxyribonucleic acid
EBV	Epstein-Barr virus
FDA	Food and Drug Administration
FIRCA	Fogarty International Research Collaboration Award, FIC
GBV-C	GB virus (hepatitis G)

GCP	Good Clinical Practices
GCRC	General Clinical Research Center
GFATM	Global Fund for AIDS, Tuberculosis, and Malaria
GI	gastrointestinal
GLP/GMP	good laboratory practice/good manufacturing practice
HAART	highly active antiretroviral therapy
HBCU	Historically Black Colleges and Universities
HBV	hepatitis B virus
HCV	hepatitis C virus
HERS	HIV Epidemiology Research Study
HHV	human herpesvirus
HIV	human immunodeficiency virus
HPTN	HIV Prevention Trial Network
HPV	human papillomavirus
HRSA	Health Resources and Services Administration
HVTN	HIV Vaccine Trials Network
IC	Institute and Center
ICC	invasive cervical cancer
IDU	injecting drug user
IRB	institutional review board
IUD	intrauterine device
JCV	JC virus
KS	Kaposi's sarcoma
KSHV	Kaposi's sarcoma herpesvirus
LRP	Loan Repayment Program, NIH
MAC	*Mycobacterium avium* complex
MDR-TB	multidrug-resistant tuberculosis
MHC	major histocompatibility complex
MSM	men who have sex with men
MTCT	mother-to-child transmission

N9	nonoxynol
NAFEO	National Association for Equal Opportunity in Higher Education
NGO	nongovernment organization
NHL	non-Hodgkin's lymphoma
NHP	nonhuman primate
NIH	National Institutes of Health
NMAC	National Minority AIDS Council
NRTIs	nucleoside reverse transcriptase inhibitors
OAR	Office of AIDS Research, NIH
OARAC	Office of AIDS Research Advisory Council
OD	Office of the Director, NIH
OI	opportunistic infection
OPHS	Office of Public Health and Science
PBMC	peripheral blood mononuclear cell
PCP	*pneumocystis carinii* pneumonia
PML	progressive multifocal leukoencephalopathy
RCMI	Research Center in Minority Institution
RCT	randomized clinical trial
RFIP	Research Facilities Infrastructure Program
RNA	ribonucleic acid
RPRC	Regional Primate Research Center
SAMHSA	Substance Abuse and Mental Health Services Administration
SCID	severe combined immunodeficiency
SHIV	chimeric simian/human immunodeficiency virus
SIT	scheduled intermittent therapy
SIV	simian immunodeficiency virus
SPF	specific pathogen-free
STD	sexually transmitted disease
STI	structured treatment interruption; sexually transmitted infection
TB	tuberculosis

Th	T helper cells
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	U.S. Agency for International Development
VEE	Venezuelan equine encephalitis virus
VRC	Vaccine Research Center
WHO	World Health Organization
WIHS	Women's Interagency HIV Study
WITS	Women and Infants Transmission Study
WRAIR	Walter Reed Army Institute for Research